Medulloepithelioma (diktyoma)

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SUMMARY

Sixteen cases of medulloepithelioma are described. Clinical data and follow-up were available on 15. Four patients underwent iridocyclectomy initially; all later needed enucleation and one had an orbital recurrence. The remaining 12 patients underwent primary enucleation. All 15 patients with follow-up are alive with no evidence of tumour recurrence. It is suggested that enucleation be performed for all but the most localised tumour. Rubeosis was noted in 13 of the 16 eyes, and this may assist in making the diagnosis. The World Health Organisation histological classification of medulloepithelioma was applied, but some problems were encountered, particularly where the presence of heteroplastic brain tissue was used as a criterion for teratoid tumour and where rosettes were used as a criterion for malignancy.

Medulloepithelioma is an uncommon tumour which arises from undifferentiated non-pigmented ciliary epithelium and which usually presents in childhood. Very rarely it may arise in optic nerve or retina. The tumour is pleomorphic and diagnosis is often delayed.

The tumour usually grows slowly and may be locally malignant. Distant metastasis is uncommon and has been described only in cases where orbital spread has occurred. Broughton and Zimmerman have contributed most to the current understanding of the clinical spectrum and histological classification of the disorder. They reviewed 56 cases derived from the records of the Armed Forces Institute of Pathology (AFIP). Clinical follow-up data were available on 33 of them. Andersen reported a series of 23 cases, about half of which were on record at the AFIP. Reese and Shields have reviewed the subject. Most other publications on medulloepitheliomas comprise single case reports with or without a review of the literature.

This paper presents the histological features of 16 cases of the tumour on record at the Institute of Ophthalmology in London. Clinical data and follow-up information were available on 15 patients. Only two of these patients have previously been the subject of case reports.

Patients and methods

Over 25 years there have been 16 cases of histologically confirmed medulloepithelioma in humans on file at the Institute of Ophthalmology for which complete biographical data are available. For the purposes of this study all tissue specimens were reviewed and fresh slides made as appropriate. Attending clinicians and pathologists were contacted for further details and current follow-up status. All but one case has been treated within the United Kingdom.

Pertinent biographical data are presented in Table 1. There were nine females and seven males. The ages at diagnosis ranged from 6 weeks to 48 years and the follow-up from three months to 25 years.

Results

CLINICAL FEATURES

The presenting symptoms are detailed in Table 2 and the pretreatment signs in Table 3. The surgical management and histological classification of the surgical specimens are recorded in Table 1. Twelve cases had primary enucleation and all were alive without clinical tumour recurrence. Three of these had extrascleral extension of the tumour, one of whom received adjuvant radiotherapy. These three patients have been followed for between 5 and 11 years.

Four patients initially had iridocyclectomies, either in order to make the diagnosis or in an attempt to excise the tumour. All four have since required enucleation—two for recurrent intraocular tumour, one for reduced vision and pain, and one for rubeotic glaucoma. One of these patients, with persistent intraocular tumour, had recurrent tumour in the
orbit two years after enucleation. This was treated with enucleation and radiotherapy. The patient had no further clinical metastasis after 11 years. The other three all had tumour cells at the site of the previous surgical section when the whole eye was examined, but the patients have remained clinically free of tumour. Two have been followed up for 11 years and one for six months.

**HISTOLOGICAL FEATURES**

Sixteen cases were reviewed. Ten were benign, of which seven were non-teratoid. Of the six malignant cases two were aggressively invasive preoperatively. Both were non-teratoid. The teratoid elements found included cartilage in three, and brain (neurones and glia) in two. Some unusual, but not teratoid, elements were also found—angioma in one and ganglion cells in another. No rhabdomyoblasts were found in any of the 16 cases. Most tumours contained rosettes of various types. Cystic change with accumulation of mucopolysaccharide material was seen in three cases. Unequivocal cytologically malignant areas contained neuroblastoma-like tissue in two, embryonal sarcoma-like tumour in one, and astrocytoma in one. Calcification was present in four cases.

**Discussion**

Medulloepithelioma was first recognised and termed ‘carcinome primitif’ by Badel and Lagrange in 1892.7 Verhoeff described another case in 1904. He gave it the name ‘teratoneuroma’, although his case contained no teratoid elements. Fuchs reported an example in 1908 in which the predominant histological feature was a net-like pattern of poorly differentiated cell ribbons, and he used the term ‘diktyoma’ derived from the Greek root for ‘net’. This name makes up brevity what it lacks in its description of cytological or embryological features, and for years was the most popular term for this tumour. The term ‘medulloepithelioma’ was first applied in 1931 by Grinker.10 The etymology of these various terms has been discussed elsewhere.1
from the ciliary epithelium has been simplified, largely through the efforts of Zimmerman. His
classification has been adopted by the World Health Organisation.11 Tumours of the ciliary epithelium are
divided into congenital (arising from undifferentiated epithelium and presenting commonly in child-
hood) and acquired (arising from differentiated epithelium and presenting commonly in adults). Un-
differentiated cells do not normally persist in the ciliary epithelium into adulthood. All congenital
ciliary epithelial tumours are medulloepitheliomas. The acquired group includes hyperplasias, adeno-
mas, and adenocarcinomas.

The diagnosis of medulloepithelioma of the ciliary body is not usually difficult histologically, and clas-
sification into the simple and elegant categories of Broughton and Zimmerman1 may prove harder. The
classification splits the tumours into benign and malignant on the basis of cytological features and
invasive, rather than metastatic, properties. The latter is not a contentious issue, since these tumours
are often locally aggressive and may spread to involve the orbit as well as other intraocular structures. The
former set of criteria, involving pleomorphism, mitotic rate, and degree of undifferentiation, are less
easy to apply, since these tumours are by definition immature and may be growing quickly. Sheets of
basaloid cells may resemble neuroblastoma or undifferentiated retinoblastoma in otherwise unre-
markable tumours. Rosetting is not necessarily a helpful diagnostic feature, since 81% of cases in the
present series had rosettes, some of the more primitive retinal alnaged type, others more like Homer-
Wright rosettes, and others with clearly delineated external limiting membranes around a central
lumen, resembling Flexner-Wintersteiner rosettes. Occasionally the rosettes have turned ‘inside-out’, and
both of the latter types of rosettes resembled those seen in dysplastic retinas, especially those
associated with trisomy 13–15.

It is interesting that heteroplastic cartilage is also
associated with this trisomy and with some micro-
phthalmic eyes. This is the most easily recognised heteroplastic or teratoid element. In the present
series only two tumours had mature cartilage. Recognition of genuinely teratoid elements can be
difficult. In several of our cases areas which appeared to be ‘brain’ were in fact composed only of gial
elements, many showing the well described spongio-
blastic change, while some appeared gemistocytic. Unequivocal neurone cell bodies were rare but were
seen in two cases. We did not regard ganglion cells as
being teratoid. Other glial concomitants such as
Rosenthal fibres were seen, and one tumour con-
tained frank astrocytomatosus areas. Rhabdomy-
blasts were seen in one specimen at the Institute of
Ophthalmology from a patient on whom biographical
data were not available, but not in any of the 16
documented cases reported here.

These tumours present a spectrum of malignancy. While most behave well, without overt aggressive
invasion, the AFIP series included four deaths from
tumour.

CLINICAL FEATURES
Rubeosis was a clinical or histological feature of 13 of
the 16 cases in this study, as compared with only 11 of
56 cases in the AFIP series. It may be a useful confrimatory sign when making the diagnosis. We
know of no work on angiogenic factors in these
tumours.

The life expectancy of treated patients is very
good. In the present series all 15 patients with follow-
up are alive, with no evidence of residual tumour. All
affected eyes had been removed, however. In the
AFIP series the presence of orbital involvement was
a major determinant of survival,1 though the present
series includes survivors even with extrascleral exten-
sion of tumours containing cytological evidence of
malignancy.

The best treatment for these patients is uncertain.
The tumour is too uncommon for any one centre to
have acquired much experience in different thera-
peutic strategies. Broughton and Zimmerman suggest that local excision be attempted for small,
well circumscribed tumours. They base this recom-
modation on two patients who had had excision
iridocyclectomies with no apparent tumour recur-
rence after a follow-up of between 1 and 22 years.
The age of the patients at treatment is not given, nor
is their subsequent visual function or the presence of
cataract, rubeosis, glaucoma, or squint. Given the
usual onset of these tumours in early childhood, one
might anticipate that such surgery would result in
significant amblyopia. Furthermore, it is not clear
whether complete excision of the tumours was
achieved: the possibility of corneoscleral extension,
which is one of the criteria of malignancy, may have
been difficult to exclude.

In the same series, eight eyes which had undergone
iridectomy or iridocyclectomy as an initial procedure
required later enucleation, making the overall
chance of retaining the eye after such surgery 20%.
The tumour is typically friable and difficult to
manipulate surgically. Although about one-half of
the tumours contain melanin pigment microscopically,1
they are often not clinically pigmented. This
makes definition of the posterior extent of the
tumour by transillumination more difficult. The
attendant rubeosis increases the risk of peroperative
intraocular haemorrhage.

Broughton and Zimmerman1 remarked on the
frequency with which highly malignant looking areas within the tumour appeared to be confined by benign tumour, and they considered that this might retard the clinical expression of malignancy. Surgical manipulation might adversely affect such a balance. The prognosis for tumours confined within the globe is uniformly excellent: no case of tumour death has been recorded without evidence of orbital involvement.

All these factors militate against attempting local excision of all but the most circumscribed tumours, given the limited chance of anatomical and functional success of the operation and the potential for promoting orbital recurrence.

We know of no data on the treatment of ocular medulloepithelioma by radiotherapy, though the central nervous system counterpart of the tumour is known to be radiosensitive. While it would be technically feasible to treat ocular medulloepithelioma by local radiotherapy employing a radioactive scleral plaque or a proton beam, the rarity of the tumour and the difficulty in establishing the diagnosis clinically would suggest that pretreatment tissue diagnosis would be required for the proper assessment of the approach. The potential hazard of intraocular biopsy of a locally aggressive tumour and the difficulty of obtaining a tissue sample representative of the entire tumour would also hamper the investigation of this option.

We recommend that enucleation should be the primary treatment for most cases. Where a credible non-neoplastic differential diagnosis exists, incisional biopsy may be considered with a view to subsequent radiotherapy for localised tumours and enucleation for extensive tumours.

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References


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